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# UNIVERSITÀ DEGLI STUDI DI TORINO

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## Age as a Long-Term Prognostic Factor in Bariatric Surgery

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### Abstract

**Objective:** To analyze the potential effects of preoperative age on postoperative weight loss in patients who underwent Roux-en-Y gastric bypass (RYGBP) with long-term follow-up data.

**Background:** The reasons for individual differences in surgically induced weight loss are not completely understood. To date, there are no available studies specifically aimed at analyzing the effects of age on weight loss in patients undergoing the same operation and with long-term follow-up data.

**Methods:** Retrospective analysis of prospectively collected data for all patients who underwent RYGBP between 2006 and 2010. To evaluate weight loss, we used preoperative and follow-up body mass index (BMI), analyzed by the mixed-effects linear model for repeated measures. To evaluate age effects, patients were classified in quartiles ( $\leq 35$  years, 36–42 years, 43–51 years,  $\geq 52$  years).

**Results:** A total of 489 patients entered the study; preoperatively, the younger group showed a significantly higher BMI (mean BMI: 48.2 in patients aged  $\leq 35$  years, 46.9 in 36–42 years, 45.5 in 43–51 years, 45.7 in  $\geq 52$  years,  $P = 0.014$ ) and a higher percentage of super-obesity (41.6% among patients aged  $\leq 35$  years, 28.1% among 36–42 years, 27.6% among 43–51 years, 28.3% among  $\geq 52$  years,  $P = 0.047$ ). In spite of this, younger patients experienced a significantly greater and prolonged BMI decrease during the entire follow-up period and the BMI trend over time resulted significantly modified according to age quartiles ( $P = 0.036$ ).

**Conclusions:** This study provides a new prognostic factor in bariatric surgery: patient age. Because advanced age represents a risk factor for complications and mortality, and given that bariatric surgery may not be as effective in older patients compared to younger subjects, we believe that surgical indications in patients older than 50 years should be carefully weighed up.

Currently, bariatric surgery has largely demonstrated to be the only long-term effective therapy for the morbidly obese population: it markedly lowers body weight, reverses or ameliorates comorbidities, improves quality of life, and ultimately results in a decrease in overall mortality.<sup>1</sup> Roux-en-Y gastric bypass (RYGBP) is the most widely performed bariatric operation,<sup>2</sup> and many studies have shown the safety and efficacy of this operation.<sup>3</sup>

Nevertheless, it is a common observation in clinical practice that postoperative weight reduction shows great disparities from one individual to another,<sup>4,5</sup> with a consistent minority of patients (5%–20%) failing to achieve successful long-term weight loss.<sup>4,6</sup>

To date, the reasons for individual differences in surgically induced weight loss are not completely understood. Different studies have compared weight loss between type of surgery<sup>7</sup> or even different techniques of the same operation,<sup>8</sup> whereas others have analyzed several preoperative predictors, with discordant results.<sup>5,9–11</sup> With regard to preoperative age, the few available published data have suggested that younger subjects could achieve a more satisfactory body weight loss, but we are unaware of studies specifically aimed at analyzing age effects on weight loss in a large cohort of patients undergoing the same operation. Furthermore, the few available data are lacking in long-term follow-up, a critical aspect in the analysis of bariatric surgery results.

Another main concern in bariatric surgery studies is that statistical evaluation of postoperative results is usually complicated by missing observations either because of dropouts or because of subjects who miss one or more visits.<sup>12,13</sup> The mixed-effects linear model for repeated measures represents a convenient statistical method that can assess changes in weight over time both within and among patients, allowing for differing numbers of data points per patient and accounting for missing values, by incorporation of all available data into a single model spanning the entire follow-up period.<sup>14</sup> These characteristics make this statistical model ideal in longitudinal bariatric surgery studies.

In the present study, we aimed to examine the role of preoperative age as a potential predictor of weight loss outcome in a group of patients who underwent RYGBP using mixed-effects linear modeling.

## **METHODS**

### **Study Population**

All patients undergoing bariatric procedures at the Minimal Invasive Surgery Center of the University of Torino are registered in a prospective Bariatric Surgery Register, in which all demographic, anthropometric, perioperative, and reintervention data, together with weight loss and comorbidity results registered during follow-up visits, are noted. We conducted a retrospective analysis of these *prospectively* collected data for all patients who underwent RYGBP at our institution between January 1, 2006, and December 31, 2010. This is a consecutive series, and no inclusion or exclusion criteria were used. All patients who entered the study had a minimum follow-up of 12 months. Follow-up data were analyzed at the reference date of December 31, 2011. All patients who underwent primary RYGBP met the US National Institutes of Health consensus statement guidelines for bariatric surgery.<sup>15</sup> For each patient, the following data were collected: gender, preoperative age, weight and height, BMI (calculated as weight in kilograms divided by height in meters squared), the preoperative presence and treatment of obesity-related comorbidities, and technical details of the surgical procedure.

### **Surgical Technique**

All the surgical procedures were performed by 2 experienced bariatric surgeons (M.T., M.M.). The RYGBP was performed using either the open or laparoscopic approach. All the pouches were created with a volume less than 30 mL and were completely divided from the gastric fundus. The Roux limb length was measured at 150 cm in all patients. The gastrojejunostomy was created using different techniques: in 96 cases, it was constructed with hand-sewn 2-layer suture with absorbable suture over a 36-Fr endoluminal bougie, whereas in 393 cases, the gastrojejunostomy was mechanically performed using a circular stapler. The anastomosis was tested for patency and leakage using methylene blue tests, and a closed suction drain was placed near the gastrojejunal anastomosis in all cases. All patients received preoperative antibiotics and low molecular-weight heparin and wore thromboembolic stockings. Patients started fluids orally by the second day, after a gastrographin swallow. All patients received proton-pump inhibitors for 6 months postoperatively.

### **Weight Loss Monitoring**

Patient follow-up was scheduled at 1 week, 30 days, 3 months, 6 months, and 12 months and annually thereafter. All patients were weighed at each visit. Preoperative weight data included height, weight, and BMI (calculated as weight in kilograms divided by height in meters squared); residual BMI was used to describe the postoperative weight loss results.

## Statistical Analysis

Prospective data were directly collected in our Bariatric Surgery Register, because no ethical approval was required for this study according to Italian law.

The primary outcome was the BMI trend over time after RYGBP and its potential modifications by 8 independent variables, measuring the BMI at several time points (3, 6, 12, 24, 36, 48, and 60 months after RYGBP) and using its repeated measures as a dependent variable in different univariate and multivariate mixed-effects linear models.<sup>14</sup>

At first, univariate analyses were performed for the following 8 independent variables: gender (male vs female); age at surgery by quartiles ( $\geq 52$  vs 43–51 vs 36–42 vs  $\leq 35$  years); preoperative BMI (classified in  $\leq 50$  and  $> 50$  kg/m<sup>2</sup>, defining the latter as the cutoff for “super-obesity”); type II diabetes (any vs none, defining the presence of diabetes as the use of oral hypoglycemic agents and/or insulin); arterial hypertension (any vs none, defining the presence of hypertension as the use of any antihypertensive medications); type of surgery (secondary vs primary RYGBP, defining the former as revisional RYGBP in previous gastric banding or vertical banded gastroplasty); surgical approach (open surgery vs laparoscopy); and gastrojejunal anastomosis (circular stapled vs hand-sewn).

The multivariate model was then estimated by the restricted maximum likelihood method and using a first-order autoregressive covariance matrix: in other words, the BMI variance at each time point was considered comparable, whereas the correlations between subsequent BMI measures similar.

The patients' characteristics were analyzed by the Fisher exact test for categorical variables and by the Mann-Whitney test for continuous ones. All reported P values were obtained by the 2-sided exact method, at the conventional 5% significance level. Data were analyzed as of January 2012 with SPSS 20.0.0 and R 2.14.1.

## RESULTS

### Patients' Baseline Characteristics

Globally, 489 patients entered the study: 376 women (76.9%) and 113 men (23.1%). The patients' baseline characteristics are summarized in Table 1.

Mean age was  $42.3 \pm 10.3$  years; age subgroups were classified in quartiles, as follows: 125 patients (25.6%) were 35 years or younger, 128 (26.2%) were aged 36 to 42 years, 123 (25.2%) were aged 43 to 51 years, and 113 (23.1%) were 52 years or older.

Mean preoperative weight and BMI were  $126.9 \pm 23.3$  kg and  $46.6 \pm 7.5$  kg/m<sup>2</sup>, respectively. Preoperative BMI was 50 kg/m<sup>2</sup> or less in 335 patients (68.5%) and greater than 50 kg/m<sup>2</sup> in 154 patients (31.5%) (Fig. 1).

Classifying patients by age quartiles, preoperative BMI was significantly higher in the younger age group: mean BMI was  $48.2 \pm 7.3$  kg/m<sup>2</sup> in patients 35 years or younger,  $46.9 \pm 7.1$  kg/m<sup>2</sup> in 36 to 42 years,  $45.5 \pm 7.7$  kg/m<sup>2</sup> in 43 to 51 years, and  $45.7 \pm 7.5$  kg/m<sup>2</sup> in patients 52 years or older, respectively ( $P = 0.014$ ).

Furthermore, the percentage of super-obese patients, that is, patients with a preoperative BMI greater than 50 kg/m<sup>2</sup>, was higher in the younger age group: super-obese patients were 41.6% among the patients 35 years or younger, 28.1% among those aged 36 to 42 years, 27.6% among those aged 43 to 51 years, and 28.3% among the patients 52 years or older, respectively ( $P = 0.047$ , Fig. 1).

Preoperative data on comorbidities were available for 451 patients; among these, 91 had type II diabetes (20.2%) and 194 had hypertension (43.0%).

The RYGBP was a primary bariatric procedure in 403 patients (82.4%) and a secondary, revisional operation in 86 (17.6%). The surgical approach was open in 46 cases, whereas 443 patients underwent laparoscopic RYGBP; among the latter, 35 (7.9%) underwent laparotomic conversion. In 96 cases (19.6%), the gastrojejunal anastomosis was hand-sewn, whereas in 393 cases (80.4%), the gastrojejunostomy was mechanically performed using a circular stapler.

### **Weight Loss and Preoperative Factors**

Follow-up ranged between 12 and 72 months, with a median value of 36 months. Follow-up rates based on the sample that reached the time points of weight measurement at the reference date of December 31, 2011, were the following: 84.3% at 3 months, 82.4% at 6 months, 84.4% at 12 months, 80.5% at 24 months, 79.1% at 36 months, 57.5% at 48 months, and 47.9% at 60 months. Rates of patients lost to follow-up at different follow-up points showed no statistically significant differences between preoperative age groups (Table 2).

Postoperative BMI showed a statistically significant time trend: median BMI was 46.9 kg/m<sup>2</sup> before surgery, 38.9 kg/m<sup>2</sup> at 3-month follow-up, 34.6 kg/m<sup>2</sup> at 6 months, 31.2 kg/m<sup>2</sup> at 12 months, 30.5 kg/m<sup>2</sup> at 24 months, 31.4 kg/m<sup>2</sup> at 36 months, 31.7 kg/m<sup>2</sup> at 48 months, and 32.7 kg/m<sup>2</sup> at 60 months ( $P < 0.001$ , Fig. 2).

The lower BMI was reached at 24 months' follow-up. At this time point, mean BMI for all patients was  $30.8 \pm 4.9$  kg/m<sup>2</sup>; classifying patients by age quartiles, mean BMIs were  $30.5 \pm 4.6$ ,  $29.9 \pm 5.2$ ,  $30.9 \pm 4.7$ , and  $32.2 \pm 4.8$  kg/m<sup>2</sup>, for patients 35 years or younger, those aged 36 to 42 years, those aged 43 to 51 years, and patients 52 years or older, respectively.

At the final follow-up time point (60 mo), mean BMI for all patients was  $32.7 \pm 6.6$  kg/m<sup>2</sup>. Classifying patients by age quartiles, mean BMIs were  $32.7 \pm 7.2$ ,  $31.4 \pm 6.2$ ,  $31.6 \pm 6.0$ , and  $36.9 \pm 6.7$  kg/m<sup>2</sup>, respectively, for each age subgroup.

In the univariate analyses, the BMI trend over time during the study period was not influenced by gender ( $P = 0.848$ ), type II diabetes ( $P = 0.355$ ), hypertension ( $P = 0.083$ ), and surgical approach ( $P = 0.459$ ), whereas it was significantly modified by age quartiles ( $P = 0.048$ ), preoperative BMI ( $P < 0.001$ ), type of surgery, that is, primary or revisional RYGBP ( $P = 0.008$ ), and type of gastrojejunal anastomosis ( $P = 0.002$ , Table 3).

In the multivariate analysis, the BMI trend over time was significantly modified only by age quartiles ( $P = 0.036$ , Table 3, Fig. 3) and baseline BMI ( $P < 0.001$ , Table 3).

## **DISCUSSION**

After RYGBP, 5% to 20% of patients do not lose weight successfully, despite standardized surgical techniques and regular follow-up.<sup>6,16,17</sup> Several preoperative predictors of poor weight loss have been studied, although most of them remain controversial, such as patient's gender<sup>8,14,18,19</sup> and the impact of obesity-related comorbidities such as diabetes mellitus.<sup>10,18-21</sup>

In the present study, to analyze the effects of demographic and operative variables on the BMI trend, we used the mixed-effects linear model for repeated measures.<sup>13,14</sup> The main finding was that BMI decrease during study period was not influenced by gender, preoperative diabetes, hypertension, or technical surgical details, whereas BMI trend over time was significantly modified by baseline BMI ( $P < 0.001$ ) and baseline age less than 52 years ( $P = 0.036$ ).

Although univariate analysis reported a difference in terms of BMI decrease based on type of surgery and type of anastomosis, both factors were not confirmed at the multivariate analysis. Thus, the results of the multivariate analysis of our data confirm the existing literature, showing that type of surgery and gastrojejunum construction do not significantly influence clinical results.<sup>22,23</sup> In line with the available published data,<sup>5,6,8,14,17,24,26</sup> super-obesity has shown in our analysis to be a strong risk factor for BMI trend over time. Even though heavier patients can lose greater absolute amounts of weight, they lose a smaller percentage of their excess weight than leaner patients,<sup>27</sup> and they tend to remain obese.<sup>14</sup>

But the most important and not yet described result of the present study was that operative age was a statistically significant modifier of the BMI trend over time. Younger patients, although significantly heavier at baseline and with a higher super-obesity incidence (42% in patients aged  $\leq 35$  years compared to 28% in the  $\geq 52$  years age group, Fig. 1), showed a lower mean BMI over time. The three youngest subgroups, i.e. patients aged from 19 to 51 years, showed a homogeneous BMI trend, whereas the older subgroup, i.e. patients aged  $\geq 52$  years, showed a significantly lower BMI decrease, with a more consistent weight regain in the long-term follow-up (Fig. 3).

The role of preoperative age in bariatric surgery was rarely investigated. In 1977, the seminal study on the gastric bypass by Printen and Mason<sup>28</sup> found that patients aged older than 50 years lost 40% less weight 2 years after surgery than younger patients. Later, in 1989, another study supported the finding of lesser weight loss in older patients, reporting a significant positive correlation between postoperative BMI and age after gastric banding.<sup>29</sup>

In the laparoscopic era, a few articles explored the relationship between preoperative age and weight loss but, although showing a trend in favor of younger patients, failed to reach any definitive conclusion because of the limited sample size or to the short follow-up.<sup>30,33</sup> Recently, a systematic review conducted with the aim of identifying preoperative predictors of weight loss following bariatric surgery has been published<sup>6</sup>; interestingly, patients' age was not included among the significant preoperative factors.

Compared with the literature data available, we believe that the present series shows consistent data on the role of older preoperative age as a negative prognostic factor, thanks to its large and homogeneous group of patients, long follow-up and high follow-up rates, and to a sophisticated statistical analysis that enables to overcome the main limitations of bariatric surgery series.

Moreover, patients lost to follow-up were equally represented among the different age groups, thus preventing selection bias.

Older age in bariatric surgery has been frequently studied as a predictor of postoperative complications, and surgical indications in the elderly people has always been a controversial topic, because the reported morbidity and mortality rates are significantly higher in older patients.<sup>9,34,36</sup> In this respect, the less satisfactory weight loss of older patients should be taken into account when discussing indications to bariatric surgery.

Different physiopathological and behavioral hypothesis may explain the relationship between age and weight loss after bariatric surgery. Energy requirements normally decrease with age.<sup>32</sup> It has been reported that, in normal body weight subjects, aging is associated with a lower lipolytic capacity,<sup>37</sup> in particular after sympathetic stimulation,<sup>38</sup> and this may explain the increased adipose tissue deposition of older subjects. Furthermore, blunted lipolytic activity has been described in obese, postmenopausal women subjected to a hypocaloric diet.<sup>39</sup> This suggests that older obese women have a decreased capacity to supply energy through the mobilization of lipids from fat stores, and this could also condition a larger caloric intake after surgery. Interestingly, younger patients have been demonstrated to have a greater reduction of energy intake after RYGBP: in a study analyzing the modifications of energy intake and their impact on body weight after RYGBP in 50 obese patients,<sup>(24)</sup> subjects younger than 35 years reduced their energy intake significantly more than those older than 35 years and showed significantly greater weight loss. From the age of 40 years, total energy expenditure begins to decline,<sup>40</sup> and this age-dependent decrease seems to be mainly due to a reduction in physical activity.<sup>41</sup> The more sedentary lifestyle

may be one reason for lower weight loss in patients older than 55 years:<sup>19,33,42</sup> younger patients may have better exercise tolerance and more active lifestyles, and successful long-term weight maintenance is known to be associated with a physically active lifestyle.<sup>43</sup> Furthermore, because obesity is not only a medical but also a social disease,<sup>44</sup> psychological and social aspects related to patient's age may account for postoperative weight loss and maintenance, because these are associated with internal motivation and social support.<sup>43</sup> It has been reported that, with respect to attractiveness, younger obese people are denigrated to a greater degree than older obese subjects;<sup>44</sup> as a result, older individuals may be less inclined to maintain lower weights. Prospective studies are needed to further elucidate the role of patient age in influencing bariatric surgery results and to define physiopathological mechanisms of age-related weight loss and maintenance.

In conclusion, this study provides a new prognostic factor in bariatric surgery: the patient's age. This finding has, in our opinion, 2 important consequences in daily clinical bariatric practice: first, it allows practitioners to provide patients with a more realistic evaluation of the potential outcomes of the procedure; second, the less satisfactory weight loss should be taken into account when evaluating surgical indications in older patients.

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Variable	N	%
N	489	
Gender		
Women	376	76.9%
Men	113	23.1%
Age (mean $\pm$ SD), years	42.3 $\pm$ 10.3	
Age subgroups, yrs		
$\leq 35$	125	25.6%
36–42	128	26.2%
43–51	123	25.2%
$\geq 52$	113	23.1%
BMI (mean $\pm$ SD), kg/m <sup>2</sup>	46.6 $\pm$ 7.5	
BMI $\leq 50$ kg/m <sup>2</sup>	335	68.5%
BMI $> 50$ kg/m <sup>2</sup>	154	31.5%
Type II diabetes		
No	360	79.8%
Yes	91	20.2%
Unknown	38	
Hypertension		
No	257	57.0%
Yes	194	43.0%
Unknown	38	
Type of surgery		
Primary RYGBP	403	82.4%
Revisional RYGBP	86	17.6%
Surgical approach		
Laparoscopy	408	83.4%
Open surgery	81	16.6%
Gastrojejunal anastomosis		
Hand-sewn	96	19.6%
Circular stapled	393	80.4%

TABLE 1 . Main Baseline Characteristics of Patients at Surgery

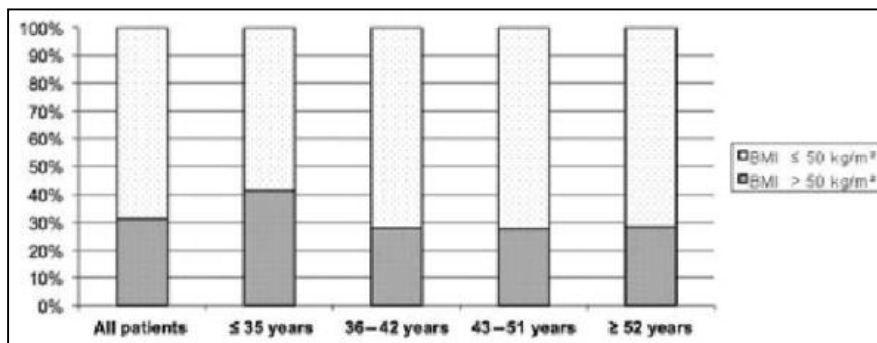


FIGURE 1 . Preoperative super-obesity incidence rates among age subgroups.

Time Point	All Patients	≤35 Years	36–42 Years	43–51 Years	≥52 Years	P
Preoperative	489	125	128	123	113	
3 months	412/489 84.3%	107/125 85.6%	107/128 83.6%	106/123 86.2%	92/113 81.4%	1.000
6 months	403/489 82.4%	101/125 80.8%	108/128 84.4%	105/123 85.4%	89/113 78.8%	0.688
12 months	413/489 84.4%	108/125 86.4%	110/128 85.9%	102/123 82.9%	93/113 82.3%	1.000
24 months	317/394 80.5%	79/106 74.5%	84/106 79.2%	82/96 85.4%	72/86 83.7%	0.277
36 months	220/278 79.1%	55/78 70.5%	57/69 82.6%	54/66 81.8%	54/65 83.1%	0.237
48 months	115/200 57.5%	34/64 53.1%	26/52 50.0%	30/44 68.2%	25/40 62.5%	0.328
60 months	68/142 47.9%	16/41 39.0%	19/39 48.7%	21/35 60.0%	12/27 44.4%	0.435

Reported follow-up rates are based on the sample, which reached the time points of weight measurement at the reference date of December 31, 2011.

TABLE 2 . Number of Available Patients and Follow-Up Rates

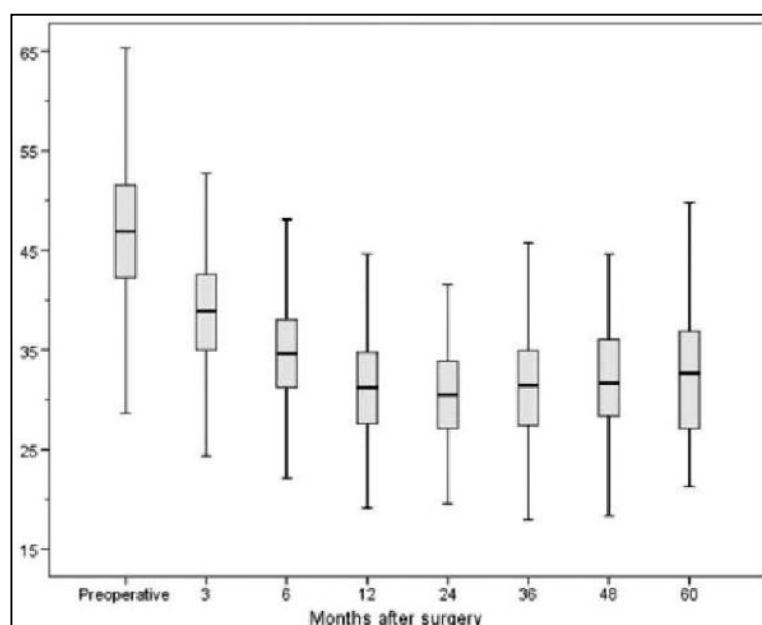


FIGURE 2 . Boxplots of BMI over time for the entire patient sample.

Variable	Univariate Analyses, <i>P</i>	Multivariate Analysis, <i>P</i>
Gender	0.848	—
Age subgroup	0.048*	0.036*
Preoperative BMI	<0.001*	<0.001*
Type II diabetes	0.355	—
Hypertension	0.083	0.283
Type of surgery	0.008*	0.161
Surgical approach	0.459	—
Gastrojejunal anastomosis	0.002*	0.307

\*Statistically significant.

TABLE 3 . Mixed Linear Models for BMI Repeated Measures From 3 to 60 Months After Surgery

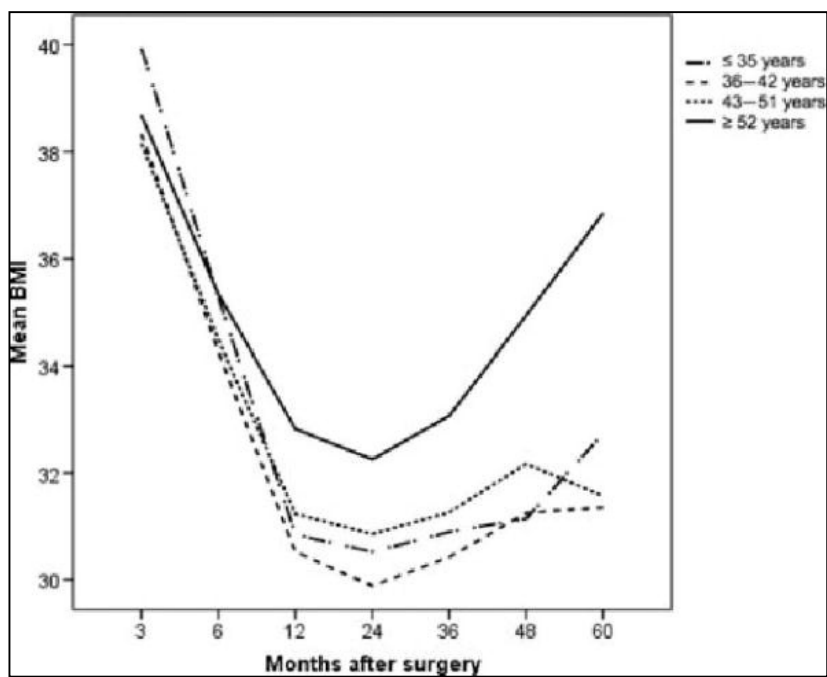


FIGURE 3 . Observed marginal means of BMI by age subgroups during the follow-up period.